

FIG. 1

BOX 1:

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Ec	(20)	DGGMGTMIQ	(SEQ ID NO: 3)
Ss	(20)	DGAMGTNLQ	(SEQ ID NO: 4)
Ml2	(5)	DGAMGTQLQ	(SEQ ID NO: 5)
Hi	(20)	DGAMGTMIQ	(SEQ ID NO: 6)
Ce	(22)	DGAMGTMIQ	(SEQ ID NO: 7)
Hs	(34)	DGGMGTMIQ	(SEQ ID NO: 8)

BOX 2:

Ec	(752)	ATVKGDVHDIGKN	(SEQ ID NO: 9)
Ss	(729)	ATVKGDVHDIGKN	(SEQ ID NO:10)
Ml2	(726)	ATVKGDVHDIGKN	(SEQ ID NO:11)
Hi	(142)	ATVKGDVHDIGKN	(SEQ ID NO:12)
Ce	(766)	ATVKGDVHDIGKN	(SEQ ID NO:13)
Hs	(778)	ATVKGDVHDIGKN	(SEQ ID NO:14)

BOX 3:

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Ec	(1095)	LAEAFAEYLH	(SEQ ID NO:15)
Ss	(1085)	MAEALAEWTH	(SEQ ID NO:16)
Ml1	(56)	LTEALAEYWH	(SEQ ID NO:17)
Hi	(490)	LAEAMAEYLH	(SEQ ID NO:18)
Ce	(1084)	LAEAYAEYLH	(SEQ ID NO:19)
Hs	(1133)	LAEAFAEELH	(SEQ ID NO:20)

BOX 4:

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Ec	(262)	GGCCGTPQHI	(SEQ ID NO:21)
Ss	(243)	GGCCGTRPDHI	(SEQ ID NO:22)
Ml2	(226)	GGCCGTPDHI	(SEQ ID NO:23)
Ce	(264)	GGCCGTPDHI	(SEQ ID NO:24)
Hs	(321)	GGCCGSTPDHI	(SEQ ID NO:25)



FIG. 3: Methionine Synthase cDNA (SEQ ID NO: 1) and amino acid (SEQ ID NO: 2) sequences.

GGTCACCTGTGGAGAGCACGTCTTCTCTGCCGCGCCCTCTGCGCAAGGAGGAGACTCGACAAC

1 ATGTCACCCGCGCTCCAAGACCTGTGCAACCCGAAGGTCTGAAGAAAACCTGCGGGATGAGATCAATGCCATTCTGCAGAAGAGGATTATGGTGTGGATGGAGGGATGGGACCATG 40
M S P A L Q D L S Q P E G L K K T L R D E I N A I L Q K R I M V L D G G M G T M

121 ATCCAGCGGGAGAAGCTAAACGAAGAACTTCCGAGGTCAGGAATTTAAAGATCATGCCAGGCCGCTGAAAGGCAACAATGACATTTAAGTATAACTCAGCCTGATGTCAATTACCAA 80
I Q R E K L N E E H F R G Q E F K D H A R P L K G N N D I L S I T Q P D V I Y Q

241 ATCCATAAGGAATACTTGTCTGGCTGGGGCAGATATCATTGAAACAAATACTTTAGCAGCACTAGTATTGCCAAGCTGACTATGGCCTGAACACTTGGCCTACCGGATGAACATGTGC 120
I H K E Y L L A G A D I I E T N T F S S T S I A Q A D Y G L E H L A Y R M N M C

361 TCTGCAGGAGTGGCCAGAAAGCTGCCAGGAGGTAACTCTCCAGACAGGAATTAAGAGGTTTGTGGCAGGGGCTCTGGGTCCGACTAATAAGACACTCTCTGTGTCCCCATCTGTGGAA 160
S A G V A R K A A E E V T L Q T G I K R F V A G A L G P T N K T L S V S P S V E

481 AGGCCGGATTATAGGAACATCACATTTGATGAGCTTGTGAAGCATACCAAGAGCAGGCCAAAGGACTTCTGGATGGCGGGTTGATATCTACTCATTGAAACTATTTTTGATACTGCC 200
R P D Y R N I T F D E L V E A Y Q E Q A K G L L D G G V D I L L I E T I F D T A

601 AATGCCAAGGCAGCTTGTTCCTCCAAATCTTTTTGAGGAGAAATATGCTCCCGGCCTATCTTTATTTACGGGACGATCGTTGATAAAAGTGGCGGACTCTTCCGGACAGACA 240
N A K A A L F A L Q N L F E E K Y A P R P I F I S G T I V D K S G R T L S G Q T

721 GGAGGGATTGTCTCAGCGTGTCTCATGGAGAACCCTCTGCATTGGATTAAATGTGCTTTGGGTGCAGCTGAGATGAGACCTTTATTGAAATAATTGAAAATGTACAACAGCC 280
G E G F V I S H G E P L C I G L N C A L G A A E M R P F I E I I G K K T T A

841 TATGTCCTCTGTTATCCCAATGCAGGCTTCCCAACACCTTTGGTGACTATGATGAAAGCCTTCTATGATGGCCAAGCACCTAAAGGATTTTGTATGGATGGCTTGGTCAATATAGTT 320
Y V L C Y P N A G L P N T F G D Y D E T P S M M A K H L K D F A M D G L V N I V

961 GGAGGATGCTGTGGGTCAACACAGATCATATCAGGGAATTGTCTGAAGCTGTGAAAAATTGTAAGCCTAGAGTTCCACCTGCCACTGCTTTTGAGGACATATGTTACTGTCTGGTCTA 360
G G C C G S T P D H I R E I A E A V K N C K P R V P P A T A F E G H M L L S G L

1081 GAGCCCTTCAGGATTGGACCGTACACCACTTTGTTAACATGGAGAGCGCTGTAATGTTGCAGGATCAAGGAAGTTTGCTAAACTCATCATGGCAGGAACTATGAAGAAGCCTTGTGT 400
E P F R I G P Y T N F V N I G E R C N V A G S R K F A K L I M A G N Y E E A L C

1201 GTTGCCAAAGTGCAGGTGGAATGGGAGCCAGGTGTTGGATGTCAACATGGATGATGGCATGCTAGATGGTCCAAGTGAATGACCAGATTTTGAACCTAATTGCTTCCGAGCCAGAC 440
V A K V Q V E M G A Q V L D V N M D D G M L D G P S A M T R F C N L I A S E P D

1321 ATCCAAAGGTACCTTTGTGCATCGACTCTCCAATTTGTCTGTGATTGAAGCTGGGTAAAGTGCTGCCAAGGGAAGTGCATTGTCAATAGCATAGTCTGAAGGAAGGAGGACGAC 480
I G A A K C I D S N F A G I V N A G I L E A G C I V N S I S L K E G E D D

1441 TTCTTGAGAAGGCCAGGAAGATTAAAGATGGAGCTGCTATGTTGGTTCATGGCTTTTGTATGAAGAAGGACAGGCAACAGAAACAGACACAAAATCAGAGTGTGACCCGGGCTTAC 520
F L E K A R K I K K Y G A A M V V M A F D E E G Q A T E T D T K I R V C T R A Y

1561 CATCTGCTTGTGAAAAAACTGGGCTTTAATCCAATGACATTATTTTTGACCCTAATATCCTAACCTTGGGACTGGAATGGAGGAACACAACCTGTATGCCATTATTTTATCCATGCA 560
H L L V K K L G F N P N D I I F D P N I L T I G T G M E E H N L Y A I N F I H A

1681 ACAAAGTCATTAAAGAAACATTACCTGGAGCCAGAATAAGTGGAGGTCTTCCAACCTTGCTCTCTCTCCGAGGAATGGAAGCCATTTCGAGAAGCAATGCATGGGTTTTCTTTAC 600
T K V I K E T L P G A R I S G G L S N L S F S F R G M E A I R E A M H G V F L Y

1801 CATGCAATCAAGTCTGGCATGGACATGGAGATAGTGAATGCTGGAACCTCCCTGTGTATGATGATATCCATAAGGAACCTCTGCAGCTCTGTGAAGATCTCATCTGGAATAAAGACCCT 640
H A I K S G D M E I V N A G I L K A A L D H K E L L Q L C E D L I W N K D P

1921 GAGGCCACTGAGAAGCTCTACGTTATGCCAGACTCAAGGCACAGGAGGGAAGAAAGTCAATCAGACTGATGAGTGGAGAAATGGCCCTGTGGAAGAAGCCCTTGAGTATGCCCTTGTG 680
E A T E K L L R Y A Q T Q G T G G K K V I Q T D E W R N G P V E E R L E Y A L V

2041 AAGGGCATTGAAAAACATATTATTGAGGATACTGAGGAAGCCAGGTAAACCAAAAAAATATCCCCGACCTCTCAATATAATTGAAGGACCCTGATGAATGGAATGAAAATTTGTTGGT 720
K G I E K H I I E D T E E A R L N Q K K Y P R P L N I I E G P L M N G M K I V G

2161 GATCTTTTGGAGCTGAAAAAATGTTTCTACCTCAGGTTATAAAGTCAGCCCGGTTATGAAGAAGGCTGTTGGCCACCTTATCCCTTTCATGGAAAAAGAGAAGAAACAGAGTG 760
D L F G A G K M F L P Q V I K S A R V M K K A V G H L I P F M E K E R E E T R V

2281 CTTAAGGCACAGTAGAAGAAGAGGACCCTTACCAGGGCACCATCGTGCTGGCCACTGTTAAAGGCGACGTGCACGACATAGGCAAGAACATAGTTGGAGTAGTCTTGGCTGCAATAAT 800
L N G T V E E E D P Y Q G T I V L A T V K G D V H D I G K N I V G V V L G C N N

2401 TTCCGATTATTGATTTAGGAGTCATGACTCCATGTGATAAGATACTGAAAGCTGCTTTGACCACAAGCAGATATAATTGGCCTGTGAGGACTCATCTCTTCCCTGGATGAAATG 840
F R V I D L G V M T P C D K I L K A A L D H K A D I I G L S G L I T P S L D E M

2521 ATTTTGTGTGCAAGGAAATGGAGAGATTAGCTATAAGGATTCCATTGTTGATTGGAGGAGCAACCACTTCAAAAAACACACAGCAGTTAAAAATAGCTCCGAGATACAGTGCACCTGTA 880
I F V A K E M E R L A I R I P L L I G G A T T S K T H T A V K I A P R Y S A P V

2641 ATCCATGTCCTGGACGCGTCCAAGAGTGTGGTGGTGTGTTCCAGCTGTTAGATGAAATCTAAAGGATGAATACTTTGAGGAAATCATGGAAGAATATGAAGATATTAGACAGGACCAT 920
I H V L D A S K S V V V C S Q L L D E N L K D E Y F E E I M E E Y E D I R Q D H

2761 TATGAGTCTCTCAAGGAGAGGAGATACTTACCCTTAAGTCAAGCCAGAAAAAGTGGTTTCCAAATGGATTGGTGTCTGAACCTCACCCAGTGAAGCCACGTTTATTTGGGACCCAGGTC 960
Y E S L K E R R Y L P L S Q A R K S G F Q M D W L S E P H P V K P T F I G T Q V

2881 TTGAAGACTATGACCTGCAGAAGCTGGTGGACTACATTGACTGGAAGCCTTCTTTGATGTCTGGCAGCTCCGGGCAAGTACCCGAATCGAGGCTTCCCAAGATATTTAACGACAAA 1000
F E D Y D L Q K L V D Y I D W K P F F D V W Q L R H D I G K N I V G V V L G C N N

3001 ACAGTAGGTGGAGAGGCCAGGAAGGTCTACGATGATGCCACAATATGCTGAACACACTGATTAGTCAAAAGAACTCCGGGCCCGGGGTGTGGTTGGGTTCTGGCCAGCACAGATATC 1040
T V G G E A R K V Y D D A H N M L N T L I S Q K K L R A R G V V G F W P A Q S I

3121 CAAGACGACATTACCTGTACGACAGGCTGCTGTGCCAGGCTGCAGAGCCATAGCCACTTCTATGGGTTAAGGCAACAGGCTGAGAAGGACTCTGCCAGCACGGAGCCATACTAC 1080
Q D D I H L Y A E A A V P Q A A E P I A T F Y G L R Q Q A E K D S A S T E P Y Y

3241 TGCCTCTCAGACTTCATCGCTCCCTTGCAATCTGGCATCCGTGACTACCTGGGCTGTTTGCCGTTGCTGTTGGGTTAGAAGAGCTGAGCAAGGCCTATGAGGATGATGGTGACGAC 1120
C L S D F I A P L H S G I R D Y L G L F A V A C F G V E E L S K A Y E D D G D D

3361 TACAGCAGCATCATGGTCAAGGCGCTGGGGGACCGGCTGGCAGAGGCCTTTGCAGAAGAGCTCCATGAAAGAGTTGCGCGAGAACTGTGGGCCTACTGTGGCAGTGAGCAGCTGGACGTC
Y S S I M V K A L G D R L A E A F A E E L H E R V R R E L W A Y C G S E Q L D V 1160

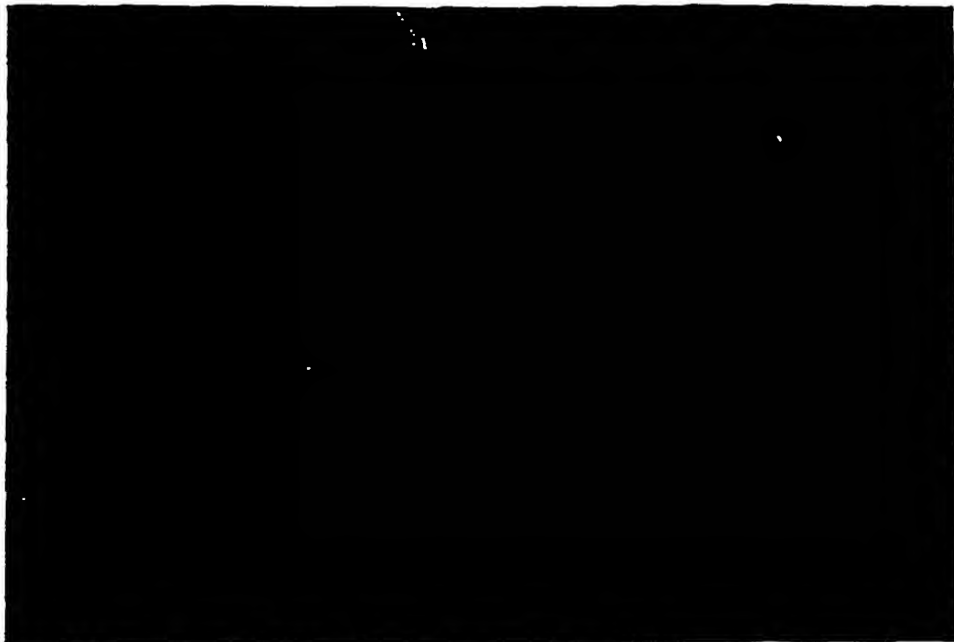
3481 GCAGACCTGCCAAGGTTGCGGTACAAGGCGATCCGCCCGGCTCCTGGCTACCCAGCCAGCCCGACCCAGAGAGCTCACCATGTGGAGACTCGCAGACATCGAGCAGTCTACAGGC
A D L R R L R Y K G I R P A P G Y P S Q P D H T E K L T M W R L A D I E Q S T G 1200

3601 ATTAGGTTAACAGAATCATTAGCAATGGCACCTGCTTCAGCAGTCTCAGGCCTCTACTTCTCCAATTTGAAGTCCAAATATTTTGCTGTGGGGAAGATTTCCAAGGATCAGGTTGAGGAT
I R L T E S L A M A P A S A V S G L Y F S N L K S K Y F A V G K I S K D Q V E D 1240

3721 TATGCATTGAGGAAGAACATATCTGTGGCTGAGGTTGAGAAATGGCTTGACCCATTTTGGGATATGATACAGACTAACTTTTTTTTTTTTTTTTGCCTTTTTTATCTTGATGATCCTCA
Y A L R K N I S V A E V E K W L G P I L G Y D T D - 1265

3841 AGGAAATACAACCTAG

FIG. 4



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FIG. 5C

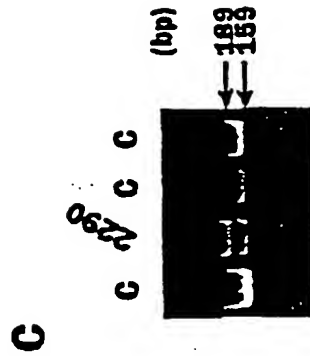


FIG. 5B

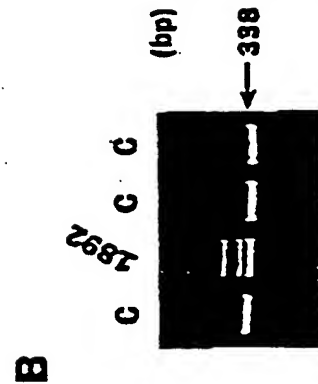
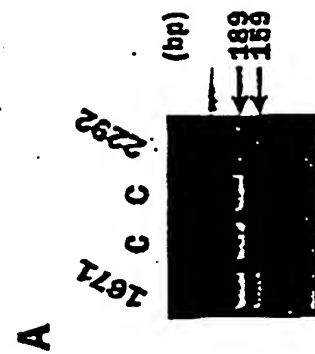


FIG. 5A



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FIG. 6

box 2

*****.* . . . * . . . * . * . . . *

Ec IATVKGDVHDIGKNIVGVVLQCNNEYIVDLGVMVPAEKILRTAKEVNADL

Hi IATVKGDVHDIGKNIVSVVMQCNNEVIDLGVMVPADKIIQTAINQKTDI

Ce IATVKGDVHDIGKNIVSVVLGCNNFKVVDLGVMTPCENIIKAAIEEKADF

Ml LATVKGDVHDIGKNLVDIILSNNGYEVVNLGIKQPITNILEVAEDKSADV

Ss IATVKGDVHDIGKNLVDIILSNNGYRVVNLGIKQPVENII EAYKKHRPDC

Mm LATVKGDVHDIGKNIVGVVLACNNFRVIDLGVMTPCDKILQAALDHKADI

Hs LATVKGDVHDIGKNIVGVVLGCNNFRVIDLGVMTPCDKILKAALDHKADI

...***. * * *...*** .. *

Ec IGLSGLITPSLDEMNVNAKEMERQG--FTIPLLIGGATTSKAHTAVKIEQNY

Hi IALSGLITPSLDEMEYFLGEMTRLG--LNLPMIGGATTSKHTAIKLYPKY

Ce IGLSGLITPSLDEMVIYVAKEMNRVG--LNIPLLIGGATTSKTHTAVKISPRY

Ml VGMSGLLVKSTVIMKENLEEMNTRGVAEKFPVLLGGAALTRS YVENDLAEVY

Ss IAMSGLLVKSTAFMKENLEVFNQEG--ITVPVILGGAALTPKFVHQDCQNTY

Mm IGLSGLITPSLDEMI FVAKEMERLA--IKIPLLIGGATTSRHTAVKIAPRY

Hs IGLSGLITPSLDEMI FVAKEMERLA--IRIPLLIGGATTSKTHTAVKIAPRY

Mutations: Δ

. * *

Ec -SGPTVYVQNASRTVGVAALLSDTQR--DDFVARTRKEYETVRIQHGRKKP

Hi KQHCVFYTSNASRAVTVCATLMNPEGR--AALWEQFKKDYEKIQQSFANSKP

Ce -PHPVVHCLDASKSVVVCSSLSDMSVR--DAFLQDLNEDYEDVRQEHYASLK

Ml -EGEVHYARDAFEGCLKLMDTIMSAK-RARRCAGEPGVLSRSPQ

Ss -KGQVIYGKDAFADLHFMDKLMPAKNSHNWDDF-QGFLGEYATE-NGHNVTTD

Mm -SAPVIHVLDASKSVVVCSQLLDENLR--DDYLEEILEEYEDIRQDHYESLK

Hs -SAPVIHVLDASKSVVVCSQLLDENLK--DEYFEEIMEEYEDIRQDHYESLK

Mutations: GD

Ec (SEQ ID NO: 73)

Hi (SEQ ID NO: 72)

Ce (SEQ ID NO: 71)

Ml (SEQ ID NO: 70)

Ss (SEQ ID NO: 69)

Mm (SEQ ID NO: 68)

Hs (SEQ ID NO: 67)